

PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:

Date of mailing **See form PCT/ISA/210**
(day/month/year)

Applicant's or agent's file reference

C 7639 / MH

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/EP2005/000751

International filing date (day/month/year)

26.01.2005

Priority date (day/month/year)

26.01.2004

International Patent Classification (IPC) or both national classification and IPC

C12Q1/68

Applicant

CLONDIAG CHIP TECHNOLOGIES GmbH

1. This opinion contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion |
| <input type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input checked="" type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/EP	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2005/000751

Box No. I

Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language
_____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material
☒ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material
☒ in written format
☒ in computer readable form
 - c. time of filing/furnishing
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☒ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2005/000751

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application
- ☒ claims Nos. 4-9 (in part), 1-10, 17, 18 (in part)

because:

- ☐ the said international application, or the said claims Nos. _____
relate to the following subject matter which does not require an international preliminary examination (*specify*):

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. 4-9 (in part), 1-10, 17, 18 (in part)

- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- ☐ has not been furnished

- ☐ does not comply with the standard

the computer readable form

- ☐ has not been furnished

- ☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2005/000751

Box No. IV

Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:
- ☐ paid additional fees
- ☐ paid additional fees under protest
- ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with
- ☒ not complied with for the following reasons:
- See supplemental sheet
4. Consequently, this opinion has been established in respect of the following parts of the international application:
- ☐ all parts
- ☒ the parts relating to claims Nos. 1-10, 17, 18 (in part)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2005/000751

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	3	YES
	Claims	1, 2, 4-10, 17, 18	NO
Inventive step (IS)	Claims		YES
	Claims	1-10, 17-18	NO
Industrial applicability (IA)	Claims	1-10, 17-18	YES
	Claims		NO

2. Citations and explanations:

Reference is made to the following documents:

- D1:** DATABASE EMBL [Online] 2 November 2001 (2001-11-02), "Sequence 35 from Patent WO0177172." XP002329868 found in EBI accession no. EM_PAT:AX280412 Database accession no. AX280412
- D2:** DATABASE MEDLINE [Online] US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; 11 March 2002 (2002-03-11), "Affymetrix GeneChip *Pseudomonas aeruginosa* Array" XP002329869 found in NCBI accession no. GPL84 Database accession no. GPL84
- D3:** WOLFGANG MATTHEW C ET AL: "Conservation of genome content and virulence determinants among clinical and environmental isolates of *Pseudomonas aeruginosa*." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 100, 14, 8 July 2003 (2003-07-08), pages 8484-8489, XP002329865 ISSN: 0027-8424
- D4:** MILLER D A ET AL: "Analysis of virulence in a multi-resistant and transmissible clone of *Pseudomonas aeruginosa* by differential genomic DNA hybridization." ABSTRACTS OF THE GENERAL MEETING OF THE AMERICAN SOCIETY FOR MICROBIOLOGY, vol. 103,

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2005/000751

Box No. V

Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement

- 2003, pages B-289 URL, XP002329866 & 103RD AMERICAN SOCIETY FOR MICROBIOLOGY GENERAL MEETING; WASHINGTON, DC, USA; MAY 18-22, 2003 ISSN: 1060-2011
- D5:** WAGNER VICTORIA E ET AL: "Microarray analysis of *Pseudomonas aeruginosa* quorum-sensing regulons: Effects of growth phase and environment." JOURNAL OF BACTERIOLOGY, vol. 185, 7, April 2003 (2003-04), pages 2080-2095 XP008047722 ISSN: 0021-9193
- D6:** DATABASE GENBANK [Online] 19 February 2003 (2003-02-19) STOVER, C.K. ET AL: "Complete genome sequence of *Pseudomonas aeruginosa* PA01, an opportunistic pathogen" XP002329870 found in GENBANK accession no. GI:9945818 Database accession no. AE004440
- D7:** WO 03/059516 A (CLONDIAG CHIP TECHNOLOGIES GMBH; SCHULZ, TORSTEN; ERMANTRAUT, EUGEN; E) 24 July 2003 (2003-07-24)

1. The present application does not meet the requirements of **PCT Article 33(1)** because the subject matter of **claims 1, 2, 4-10, 17 and 18** is not novel under **PCT Article 33(2)**: documents **D1-D5** are novelty-destroying with respect to **claims 1, 2, 4-10, 17 and 18**; see the full document in each case. **D1** contains an oligonucleotide which has 83% sequence identity with SEQUENCE NUMBER 1 and is therefore novelty-destroying with respect to claim 1(ii) and (iv).
2. The present application does not meet the requirements of **PCT Article 33(1)**, because the subject matter of **claims 1-10, 17 and 18** does not

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2005/000751

Box No. V

Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement

involve an inventive step under **PCT Article 33(3)**:
in addition to **claims 1, 2, 4-10, 17 and 18** attacked
by documents **D1-D5** which are prejudicial to novelty,
the remaining dependent **claim 3** does not contain any
features which, in combination with the features of
any claims to which it refers back, meet the **PCT**
requirements for novelty and inventive step. The
device addressed in **claim 3**, for example, is
described as known in the description of the present
application and identified with document **D7**.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2005/000751

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

- 1 Contrary to **PCT Rule 5.1(a)(ii)**, the description of the present patent application does not mention **D1** to **D6** or otherwise indicate the relevant prior art disclosed therein.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Box IV

This Authority has established that the international application contains several inventions which are not linked by a single general inventive concept (PCT Rule 13.1), specifically:

Invention 1, claims 1-10, 17, 18 (in part):

Oligonucleotide of line 1 under point (i.) of claim 1, microarray device using this oligonucleotide and use of this oligonucleotide for detecting bacterial strains of the *Pseudomonas aeruginosa* species and for genotyping and pathotyping *Pseudomonas aeruginosa*.

Inventions 2-114, claims 1-10, 17, 18 (in part):

Oligonucleotide of lines 2 to 114 under point (i.) of claim 1, microarray device using this oligonucleotide and use of this oligonucleotide for detecting bacterial strains of the *Pseudomonas aeruginosa* species and for genotyping and pathotyping *Pseudomonas aeruginosa*.

Inventions 115-274, claims 11-19 (in part):

Oligonucleotide of lines 115-274 under claim 16, process for specific detection of bacterial strains, use of this oligonucleotide for detecting bacterial strains of the *Pseudomonas aeruginosa* species, for genotyping and pathotyping this organism and use of the primer for

Supplemental Box

amplifying nucleic acids of bacterial strains of this species.

The reasons are as follows:

The **general concept** of the present application is that of oligonucleotides for genotyping the *Pseudomonas aeruginosa* species. This general concept, however, is known from the prior art. The authors in **D3** utilize a DNA microarray of the full genome of *P. aeruginosa* in order to detect the genomic variability of the various *P. aeruginosa* strains. In this analysis, 18 different strains of *P. aeruginosa* are used. With the aid of this microarray, the 18 different strains are identified and assigned phylogenetically; see in particular figure 2. In addition, the description for a biochip from Affymetrix (**D2**) can be found in the prior art. This document bears the title "Affymetrix GeneChip *Pseudomonas aeruginosa* Array/Platform GPL84" and describes such a biochip from 19.02.2002. The accompanying data sheet from Affymetrix describes the biochip in more detail and stresses that the chip contains approx. 5500 oligonucleotides of a length of 25 base pairs which are derived from various strains of the *Pseudomonas aeruginosa* species. This biochip likewise finds use in prior art **D5**. **D4** likewise contains the general concept of the invention.

In summary, the general concept of the present application is known from the prior art and the ISA is of the opinion that the present application lacks a uniform inventive concept, which has the consequence that there is lack of unity under **PCT Rule 13.1**. Consequently, every single oligonucleotide listed in claims 1 and 16 embodies

Supplemental Box

an alternative solution to the prior art. With regard to the prior art, the different inventions are therefore not linked by a general inventive concept and are listed separately in the opinion in accordance with **Article 17(3) (a)**. This leads to the presence of a total of **274 different inventions**.

A restriction of the claims to one of the aforementioned inventions has not taken place, and the applicant has chosen not to pay additional fees. Consequently, the subject matter of the examination in the present written opinion of the International Search Authority is restricted to the first invention formulated above, which has the following wording:

Invention 1, claims 1-10, 17, 18 (in part):

Oligonucleotide of line 1 under point (i.) of claim 1, microarray device using this oligonucleotide and use of this oligonucleotide for detecting bacterial strains of the *Pseudomonas aeruginosa* species and for genotyping and pathotyping *Pseudomonas aeruginosa*.